> [t]he specification shall contain a written description of the invention, and of the manner and process of making an using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same . . . .

Applicants respectfully submit that the claims 19 and 20, as amended, recite subject matter that is enabled by the specification provided in the present application. Specifically, Applicants respectfully submit that the specification provides a written description of the invention that enables any person of skill in the art to make and use the subject matter recited in amended claims 19 and 20. Therefore, Applicants respectfully request that the rejection of claims 19 and 20 under 35 U.S.C. § 112, first paragraph, be withdrawn.

Claims 1, 2, 5 through 15, and 18 stand rejected under 35 U.S.C. § 112, second paragraph. However, because claims 1, 2, 5 through 15, and 18 are cancelled herein without prejudice or disclaimer, such rejection is no longer relevant, and Applicants respectfully request that the rejection be withdrawn.

Finally, claims 1, 2, 5 through 15, and 18 through 20 stand rejected under 35 U.S.C. § 112, second paragraph. However, because claims 1, 2, 5 through 15, and 18 are cancelled herein without prejudice or disclaimer, such rejection is discussed only as it relates to claims 19 and 20.

Applicants respectfully submit that the rejection of claims 19 and 10 under 35 U.S.C. § 112, second paragraph, should be withdrawn. The second paragraph of 35 U.S.C. § 112 requires that "[t]he specification . . . conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention." In this case, Applicants respectfully submit that claims 19 and 20, as amended, particularly point out and distinctly claim subject matter which Applicants regard as their invention. Thus, Applicants respectfully submit that the rejection of claims 19 and 20 under 35 U.S.C. § 112, second paragraph, be withdrawn.

35 U.S.C. § 103(a) Obviousness Rejections

Claims 1, 2, 5 through 15 and 18 through 20 stand rejected under 35 U.S.C. § 103(a) ("Section 103") as being unpatentable over the combined teachings of Edgren et al. (U.S. Patent 4,931,285), Oshlack et al. (U.S. Patent 6,024,982), Baichwal (U.S. Patent 5,455,046), and

Svastano et al. (U.S. Patent 5,681,584). However, because claims 1, 2, 5 through 15, and 18 are cancelled herein without prejudice or disclaimer, Applicants address the rejection under Section 103 only as it applies to claims 19 and 20.

Applicants respectfully submit that the rejection of claims 19 and 20 under Section 103 should be withdrawn. A rejection under Section 103(a) is improper and will be overturned unless a *prima facie* case of obviousness is established against the rejected claims. *In re Rijckaert*, 9 F.3d 1531, 1532, 28 U.S.P.Q.2d 1955, 1956 (Fed. Cir. 1993). Applicants respectfully submit that the combined teachings of the references cited in the Final Office Action fail to establish the *prima facie* obviousness of any of the claims now pending. Therefore, Applicants respectfully request that the rejections of claims 19 and 20 under Section 103 be withdrawn.

As is set forth in M.P.E.P. 706.02(j), a *prima facie* case of obviousness under Section 103 can not be established unless three criteria are met:

> First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

The examiner bears the burden of establishing these three criteria based on the prior art. Significantly, this burden can be met "only by showing some objective teaching in the prior art or that knowledge generally available to one of ordinary skill in the art would lead that individual to combine the relevant teachings of the references." *In re Fritch*, 972 F.2d 1260, 1265, 23 USPQ2d 1780, 1783 (Fed. Cir. 1992) (emphasis added).

In this case, Applicants respectfully submit that the combined teachings of the cited references do not teach or suggest each of the limitations recited in claims 19 and 20, as amended. In particular, Applicants respectfully submit that the cited references do not teach or suggest a dosage form including an interior and an exterior membrane, as they are defined in

claim 19, with the interior membrane being formed around a core comprising a drug formulation. Therefore, Applicants respectfully submit that the combined teachings of the references cited in the Office Action do not teach or suggest each of the limitations recited in claim 19, as amended, or claim 20, as amended, which depends from claim 19, applicants respectfully request that the rejection of claims 19 and 20 under Section 103 be withdrawn.

Conclusion

Applicants respectfully submit that the amendments set forth herein place the case in condition for allowance, and an early notice thereof is respectfully solicited. Should the Examiner determine that additional issues remain which might be resolved by a telephone conference, he is respectfully invited to contact Applicants' undersigned attorney.

Respectfully Submitted,

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Enclosures: Version with Markings to Show Changes Made

SEW/eg

Date: October 17, 2001

Version with Markings to Sh w Changes Made

Please cancel claims 1, 2, 5 through 15, and 18 without prejudice or disclaimer.

Please amend the following claims as follows:

19. (Amended) A dosage form comprising:

a core comprising a drug formulation;

[a first membrane and a second membrane; said first membrane] an interior membrane formed around the core, the interior membrane comprising 35 wt% to 70 wt% of a polymer possessing a lipophilic-attracting property, 25 wt% to 65 wt% of a flux enhancer, and 0 wt% to 10 wt% of a surfactant; and

[said second membrane] an exterior membrane formed around the interior membrane, the exterior membrane comprising 35 wt% to 70 wt% of a polymer permeable to the passage of an aqueous fluid, 10 wt% to 40 wt% of a plasticizer, 20 wt% to 35 wt% of a peptide, and 0 wt% to 10 wt% of a surfactant[; 100 ng to 750 mg of a drug in the dosage form; and wherein, when the dosage form is in use, the drug is delivered over a sustained-release time up to thirty hours].

20. (Amended) The dosage form [according to] of claim 19, wherein[;] the [first] interior membrane contacts the [second] exterior membrane, and an exit is present in the [contacting] interior and exterior membranes for delivering the drug from the dosage form.

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Please add the following new claims:

21. A sustained release dosage form comprising:

a core formulation; and

a bilayer membrane formed around the core formulation, the bilayer membrane comprising:

an interior lipophilic membrane; and

an exterior hydrophilic membrane comprising a compound possessing at least one peptide moiety, the exterior membrane being formulated to delay the disintegration of the interior membrane.

22. The sustained release dosage form of claim 21, wherein the exterior hydrophilic membrane comprises:

20 wt % to 35 wt% of the compound possessing at least one peptide moiety;

35 wt% to 70 wt% of a semipermeable polymer;

10 wt% to 40 wt% of a plasticizer; and

0 wt% to 10 wt% of a surfactant.

23. The sustained release dosage form of claim 21, wherein the hydrophilic exterior membrane comprises:

20 wt% to 35 wt% of the compound possessing at least one peptide moiety;

35 wt% to 70 wt% of a member selected from the group consisting of a cellulose acylate, cellulose diacylate, and a cellulose triacylate polymer;

10 wt% to 40 wt% of a plasticizer that increases the aqueous diffusion coefficient of the exterior hydrophilic membrane and is selected from the group consisting of glycerin, triacetin, adipic acid, azelaic acid, citric acid, triethyl citrate, acetyl triethyl citrate, tributyl citrate, acetyl tributyl citrate, butyryl trihexyl citrate, polyethylene glycol, diethylene glycol dipelargonate and triethylene glycol di(2-ethylbutrate); and

0 wt% to 10 wt% of a surfactant.

Versi n with Markings to Sh w Changes Made

24. The sustained release dosage form of claim 21, wherein the compound possessing at least one peptide moiety comprises 20 wt% to 35 wt% of the exterior membrane and comprises a protein possessing a molecular weight of 1500 to 350,000.

25. The sustained release dosage form of claim 22, wherein the surfactant is selected from the group consisting of an anionic, amphoteric, cationic and nonionic surfactant.

26. The sustained release dosage form of claim 21, wherein the compound possessing at least one peptide moiety comprises a member selected from the group consisting of reticulin, silk, keratin, casein, lactoglobulin, prolamine, gluten, albumin, elastin, soy protein, globulin, gelatin, collagen, and zein.

27. The sustained release dosage form of claim 24, wherein the protein is sized between about 0.1 microns to 50 microns in one dimension.

28. The sustained release dosage form of claim 21, wherein the interior lipophilic membrane comprises:

35 wt% to 70 wt% of a lipophilic polymer;

25 wt% to 65 wt% of a flux enhancer; and

0 wt% to 10 wt% of a surfactant.

29. The sustained release dosage form of claim 28, wherein the lipophilic polymer comprises poly(ethyl cellulose).

30. The sustained release dosage form of claim 28, wherein the flux enhancer comprises hydroxyalkylcellulose, wherein the alkyl group comprises 1 to 6 carbon atoms.

31. The sustained release dosage form of claim 28, wherein the lipophilic polymer comprises poly(ethyl cellulose) exhibiting a viscosity of 3 to 350 centipoise.

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32. The sustained release dosage form of claim 28, wherein the flux enhancer comprises a hydroxyalkylcellulose selected from the group consisting of hydroxyethylcellulose and hydroxypropylcellulose.

33. The sustained release dosage form of claim 28, wherein the surfactant comprises a member selected from the group consisting of polyoxyl 4 stearate, polyoxyl 8 stearate, polyoxyl 20 stearate, polyoxyl 30 stearate, polyoxyl 40 stearate, polyoxyl 50 stearate, polyoxyl 100 stearate, polyoxyl 4 distearate and polyoxyl 150 distearate, and wherein the number refers to the surfactant polymer length in oxyethylene units.

34. The sustained release dosage form of claim 21, further comprising an exit through the bilayer membrane for delivering the drug from the dosage form.

35. The sustained release dosage form of claim 21, wherein the core formulation comprises a drug.

36. The sustained release dosage form of claim 21, wherein the core formulation comprises a drug and an expandable composition.